September 9, 1947

Dr. E. C. Kleiderer
Lilly Research Laboratories
Indianapolis 6, Indiana

Dear Dr. Kleiderer:

I am glad to report that I got back safely after a two-months' trip to England and Sweden. My wife and I went by air, and enjoyed the traveling very much, as well as our visits in Stockholm, London, Cambridge, and Oxford.

I am looking forward to seeing you next month, sometime between the 10th and 25th of October. I shall plan to come to Indianapolis, for two or three days, in case that this is satisfactory with you. It will be a pleasure to see how the work in the Lilly Laboratories has been going on.

The question of a research program on insulin here in the Gates and Crellin Laboratories has been on my mind, and I have also talked with Professor Niemann and Professor Beadle about it. I am sure that as time went on there would be a number of interesting things that we could try with insulin. In particular, our program of structural studies of amino acids and proteins has been moving along very well, although necessarily rather slowly because of the great difficulty of the work.

One idea that I have had, and would like to try out sometime if possible, is that of making an investigation of the fate of insulin in the body. It seems surprising to me that insulin retains its activity in the blood stream for such a short while after injection or release. There is, of course, a sound physiological reason for this, in normal healths, but if it were possible to retain the activity for a longer period a patient might well be able, by ingesting at smaller suitable intervals, to make a given amount of insulin last very much longer than at present. In view of what you and Dr. Clowes told me a few months ago, this possibility should, I think, be investigated.

One suggestion that I have to make, and which I think either you or we might follow up, is to attempt to change the insulin molecule in such a way as to cause it to retain its activity but to be stabilized, so that it remains active in the blood stream for a longer time. I would suggest that insulin be treated with various reagents - ketene, carbon suboxide, etc. - in order to find out whether such chemical treatment can be carried out without destroying the activity of the insulin, and what the effect of the chemical treatment is on the period of activity. There is a chance - a small chance, it is true - that a chemically treated insulin might be manufactured that would

be many times more effective than ordinary insulin.

Please let me know what you think of this idea. I shall continue to spend some time on the insulin problem, in the hope of finding promising methods of attack on it.

Sincerely yours,

Linus Pauling"W